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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,995	07/09/2001	Didier Branellec	ST98032	1245

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EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1636	17

DATE MAILED: 07/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)	
09/787,995	BRANELLEC ET AL	
Examiner	**Art Unit**	
Maria B Marvich, PhD	1636	

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,19 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 May 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This office action is in response to an amendment filed 5/6/03,Paper No. 17. Claims 17-18 have been canceled and claims 19-20 have been added. Claims 1-16 have been amended. Claims 1-16 and 19-20 are pending. There is a new ground of rejection herein and therefore, this rejection is not final.

Response to Amendment

Receipt of formal drawings is acknowledged.

Receipt of the substitute specification and the statement that the substitute specification contains no new matter is acknowledged. The substitute specification and abstract have been entered but not the substitute claims.

The objection to claim 16 as being in improper form is withdrawn in light of amendment to claim.

Rejection of claims 1-6, 8, 10-12, 14, 17 and 18 under 35 U.S.C. 102(a) as being anticipated by Schwartz et al., (WO 93/09236) is withdrawn in light of amendments to claims. Specifically, the claims have been amended to recite that the hybrid promoter comprises an enhancer region of a strong and ubiquitous promoter/enhancer. Schwartz et al. do not teach use of an enhancer region of a strong and ubiquitous promoter/enhancer in addition to a promoter that directs expression in smooth muscle cells.

Rejection of claims 1-11,15, 17 and 18 under 35 U.S.C. 102(e) as being anticipated by Leiden et al, US 6,297,220 is withdrawn in light of amendment to claims. Specifically, the claims have been amended to recite that the hybrid promoter comprises an enhancer region of a strong and ubiquitous promoter/enhancer. Leiden et al. do not teach use of an enhancer region of a strong and ubiquitous promoter/enhancer in addition to a promoter that directs expression in smooth muscle cells.

Rejection of claims 1-6, 8, 10-12, 14, 17 and 18 under 35 USC 102(b) as being anticipated by Coleman et al. is withdrawn in light of amendment to claims. Specifically, the claims have been amended to recite that the hybrid promoter comprises an enhancer region of a strong and ubiquitous promoter/enhancer within 1 kb of each other. While Coleman et al. teach use of a promoter that directs expression in smooth muscle cells that can be used by itself or in combination with e.g. enhancers, there is no discussion as to proximity of the promoter and enhancer or of the specific type of enhancers contemplated.

Rejection of claims 1- 18 under 35 U.S.C. 112, second paragraph, is withdrawn in light of amendment to claims. Specifically, claims 1-16 have been amended and claims 17-18 have been cancelled. As well, rejection of claims 1-18 because of use of the word "strong" is withdrawn upon reconsideration.

Drawings

The drawings are objected to as there is no brief description of Figure 6.

Abstract

The substitute abstract is objected to as a period appears in the middle of the sentence on line 2.

Claim Rejections - 35 USC § 102

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 4, 7-16 and 19-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Antelman et al. US 6,074,850 (Jun. 13, 2000 filed Feb 14, 1997). **This rejection is maintained for reasons of record filed 1/2/03, Paper No. 11 and restated below. This rejection is extended to claim 16 and newly added claims 19-20.**

Antelman et al. teach a viral vector or plasmid for tissue specific expression of an E2F-Rb fusion construct (column 15, line 5-9). This fusion contains genes able to induce apoptosis, modify proliferation and that function as transcription factors. This plasmid, pASN286-56, contains the adenovirus type 5 inverted terminal repeat (ITR), packaging signals and an E1A enhancer followed by the human smooth muscle α-actin promoter and a 286-56 cassette

(containing the fusion of E2f and Rb) followed by the E1b/proteinIX poly A signal (column 15, line 26-31). Antleman et al. teach pharmaceutical formulations for the administration of the adenovirus by formulation of liposome suspensions acceptable for intravenous or local or topical administration (column 10, line 35-64).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-16 and 19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Antelman et al. US 6,074,850 (Jun 13, 2000) in view of Boshart et al. Cell (1985) 41:521-530. **This is a new rejection.**

Applicants claim a hybrid promoter comprising an enhancer region and a promoter region that directs high expression in smooth muscle cells. The enhancer is selected from the group consisting of the CMV enhancer region, the RSV-LTR enhancer region SV40 enhancer region and the EF1α enhancer region.

Antelman et al. teach a viral vector or plasmid for tissue specific expression of an E2F-Rb fusion construct (column 15, line 5-9). This fusion contains genes able to induce apoptosis, modify proliferation and that function as transcription factors. This plasmid, pASN286-56, contains the adenovirus type 5 inverted terminal repeat (ITR), packaging signals and an E1A enhancer followed by the human smooth muscle α-actin promoter and a 286-56 cassette

(containing the fusion of E2f and Rb) followed by the E1b/proteinIX poly A signal (column 15, line 26-31). Antleman et al. teach pharmaceutical formulations for the administration of the adenovirus by formulation of liposome suspensions acceptable for intravenous or local or topical administration (column 10, line 35-64). The primary reference does not teach use of the CMV enhancer in the smooth muscle cell specific vector, pASN286-56, which utilizes the E1A enhancer.

Boshart et al teach isolation and characterization of the CMV enhancer. The CMV enhancer was found to be the strongest enhancer analyzed (page 42, column 2, first paragraph). Boshart et al. found that the enhancer has little cell-type or species preference for enhancement of expression and is a useful component of eukaryotic expression vectors (abstract). This was shown by enhanced expression of rabbit β-globin using the CMV enhancer. Therefore, the CMV enhancer, similar to the E1A enhancer, enhances expression of heterologous genes in a strong and ubiquitous manner.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the E1A enhancer in the expression vector taught by Antelman et al. with the CMV enhancer taught by Boshart et al. because Antelman et al. teach that it is within the ordinary skill of the art to use a smooth muscle specific vector and because Boshart et al. teach that it is within the ordinary skill of the art to use a CMV enhancer as a heterologous enhancer. One would have been motivated to do so in order to receive the expected benefit of enhanced expression from pASN286-56 by the use of the CMV enhancer in the vector. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent

evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to Arguments

On page 12-13 of the amendment filed 5/6/03, Paper No. 16, applicant traverses the rejection of claims 1-15 and 17-18 under 35 U.S.C. 102(e) as being anticipated by Antleman et al, US 6,074,850. Applicant argues that Antleman et al. do not teach any a hybrid promoter as disclosed in the instant application. Furthermore, applicant argues that Antleman et al. are silent with respect to the location of the promoter and the enhancer, which according to the instant invention are <1 kb apart. Applicant further states that the passage that is quoted is devoid of any teachings regarding the locations of the enhancer and the promoter.

Applicant's arguments filed 5/6/03 have been fully considered but they are not persuasive as regards the rejection of claims 1, 4, 7-16 and 19-20 as anticipated by Antelman et al. A passage cited (column 15-18) in the original office action filed 1/2/03, Paper No. 11, contains the following statement "This plasmid (pASN286-56) consisted of the adenovirus type 5 inverted terminal repeat (ITR), packaging signals and E1a enhancer, followed by the human smooth muscle α-actin promoter an, 286-56 cassette, and then Ad 2 sequence 4021-10462 (which contains the E1b/protein IX poly A signal) in a pBR322 background." (column 15,line 26-31). Absent evidence to the contrary, this plasmid contains a hybrid promoter that comprising an enhancer and the human smooth muscle α-actin promoter with no intervening sequences and therefore are less than 1 kb apart. Therefore, the plasmid of Antleman et al. meets the limitations of the instant invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (703) 605-1207. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, Zeta Adams, whose telephone number is (703) 305-3291.

Maria B Marvich, PhD
Examiner
Art Unit 1636

July 25, 2003

TERRY MCKELVEY
PRIMARY EXAMINER